

TK13152

Page: 7

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	CHO (mg/dL)					TG (mg/dL)				
	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	146	144	158	158	162	35	31	32	26	23
RP1F02	120	125	132	138	134	23	26	51	21	24
RP1F03	161	158	157	157	168	12	18	16	16	18
RP1F04	105	112	105	109	103	30	44	18	26	28
Mean	133	135	138	141	142	25	30	29	22	23
S.D.	25	20	25	23	30	10	11	16	5	4
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	PL (mg/dL)					IP (mg/dL)				
	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	196	180	206	189	191	3.93	4.16	3.84	4.48	4.26
RP1F02	167	182	217	194	211	4.67	3.98	3.54	3.85	4.28
RP1F03	203	205	216	210	227	4.31	4.00	4.12	4.45	3.82
RP1F04	181	212	185	190	179	2.81	3.43	4.18	3.13	4.03
Mean	187	195	206	196	202	3.93	3.89	3.92	3.98	4.10
S.D.	16	16	15	10	21	0.81	0.32	0.29	0.64	0.22
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 9

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	CA (mg/dL)					NA (mEq/L)				
	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	9.51	9.76	9.18	9.49	9.07	152.5	149.3	143.7	150.9	147.8
RP1F02	10.24	9.97	9.52	9.60	9.62	151.7	148.4	143.3	148.9	145.3
RP1F03	10.21	10.57	10.33	10.15	9.81	151.9	153.9	149.6	155.2	150.7
RP1F04	9.77	10.14	9.50	9.29	9.52	151.2	150.2	145.6	148.0	146.5
Mean	9.93	10.11	9.63	9.63	9.51	151.8	150.5	145.6	150.8	147.6
S.D.	0.35	0.34	0.49	0.37	0.31	0.5	2.4	2.9	3.2	2.3
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	K (mEq/L)					CL (mEq/L)				
	K (mEq/L)	K (mEq/L)	K (mEq/L)	K (mEq/L)	K (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	3.92	4.90	4.52	4.30	3.98	111.0	107.3	106.9	111.8	107.3
RP1F02	4.50	4.44	4.12	4.29	4.07	115.7	106.6	108.5	113.4	108.9
RP1F03	3.88	4.52	4.49	4.18	3.95	108.7	104.7	108.4	111.6	106.5
RP1F04	3.87	4.20	4.71	3.66	4.02	115.5	107.9	110.8	114.8	110.4
Mean	4.04	4.52	4.46	4.11	4.01	112.7	106.6	108.7	112.9	108.3
S.D.	0.31	0.29	0.25	0.30	0.05	3.5	1.4	1.6	1.5	1.7
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 11

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	TP (g/dL)					ALB (g/dL)				
	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	7.22	7.16	6.85	6.86	6.69	4.08	4.05	3.95	4.10	3.85
RP1F02	7.56	7.41	7.03	7.14	7.29	4.20	4.05	3.88	3.93	3.98
RP1F03	8.24	8.02	7.62	7.66	7.43	4.56	4.37	4.27	4.43	4.19
RP1F04	7.71	7.77	7.20	7.15	7.31	4.02	4.06	3.87	3.89	3.79
Mean	7.68	7.59	7.18	7.20	7.18	4.22	4.13	3.99	4.09	3.95
S.D.	0.42	0.38	0.33	0.33	0.33	0.24	0.16	0.19	0.25	0.18
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	A/G					T-BA ($\mu\text{mol/L}$)				
	A/G	A/G	A/G	A/G	A/G	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	1.30	1.30	1.36	1.49	1.36	3.8	3.9	5.2	2.7	3.0
RP1F02	1.25	1.21	1.23	1.22	1.20	1.0	2.2	41.1	3.1	43.9
RP1F03	1.24	1.20	1.27	1.37	1.29	1.3	0.5	3.6	1.0	1.5
RP1F04	1.09	1.09	1.16	1.19	1.08	1.8	1.0	2.0	2.0	2.4
Mean	1.22	1.20	1.26	1.32	1.23	2.0	1.9	13.0	2.2	12.7
S.D.	0.09	0.08	0.08	0.14	0.12	1.3	1.5	18.8	0.9	20.8
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	CRP (mg/dL)				
	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)
	-1	1	2	3	4
RP1F01	0.08	0.07	0.11	0.07	0.08
RP1F02	0.02	0.03	0.05	0.09	0.06
RP1F03	0.08	0.11	0.13	0.11	0.13
RP1F04	0.15	0.24	0.23	0.30	0.21
Mean	0.08	0.11	0.13	0.14	0.12
S.D.	0.05	0.09	0.07	0.11	0.07
N	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	AST (U/L)					ALT (U/L)				
	AST (U/L)	AST (U/L)	AST (U/L)	AST (U/L)	AST (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	23	28	35	26	27	25	40	50	41	44
RP2F02	30	39	29	40	34	28	38	37	35	44
RP2F03	22	20	23	22	20	26	27	23	30	31
RP2F04	18	16	18	22	22	27	25	28	43	48
Mean	23	26	26	28	26	27	33	35	37	42
S.D.	5	10	7	9	6	1	8	12	6	7
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 15

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	ALP (U/L)					LD (U/L)				
	ALP (U/L)	ALP (U/L)	ALP (U/L)	ALP (U/L)	ALP (U/L)	LD (U/L)	LD (U/L)	LD (U/L)	LD (U/L)	LD (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	723	657	638	725	686	264	343	241	231	205
RP2F02	648	1092	1335	1151	1133	316	373	298	316	257
RP2F03	643	939	1016	934	884	234	230	240	217	187
RP2F04	779	974	861	830	777	232	171	202	213	205
Mean	698	916	963	910	870	262	279	245	244	214
S.D.	65	184	293	182	193	39	95	40	48	30
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	CK (U/L)					GGT (U/L)				
	CK (U/L)	CK (U/L)	CK (U/L)	CK (U/L)	CK (U/L)	GGT (U/L)	GGT (U/L)	GGT (U/L)	GGT (U/L)	GGT (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	61	57	105	77	63	39.9	42.0	42.8	40.9	42.1
RP2F02	123	173	238	247	259	37.8	36.6	34.5	32.5	32.7
RP2F03	80	71	72	76	79	44.0	40.0	41.2	41.7	40.3
RP2F04	79	54	77	96	80	40.5	32.3	31.3	33.4	32.4
Mean	86	89	123	124	120	40.6	37.7	37.5	37.1	36.9
S.D.	26	57	78	83	93	2.6	4.2	5.5	4.8	5.0
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 17

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	GLDH (U/L)					LAP (U/L)				
	GLDH (U/L)	GLDH (U/L)	GLDH (U/L)	GLDH (U/L)	GLDH (U/L)	LAP (U/L)	LAP (U/L)	LAP (U/L)	LAP (U/L)	LAP (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	17	32	46	29	32	45	43	47	44	44
RP2F02	14	13	7	9	11	44	47	45	43	41
RP2F03	10	10	9	14	17	38	34	35	36	33
RP2F04	6	9	11	13	25	93	53	51	54	57
Mean	12	16	18	16	21	55	44	45	44	44
S.D.	5	11	19	9	9	26	8	7	7	10
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	GLU (mg/dL)					BIL (mg/dL)				
	GLU (mg/dL)	GLU (mg/dL)	GLU (mg/dL)	GLU (mg/dL)	GLU (mg/dL)	BIL (mg/dL)	BIL (mg/dL)	BIL (mg/dL)	BIL (mg/dL)	BIL (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	86	80	80	78	84	0.19	0.17	0.10	0.17	0.09
RP2F02	89	92	131	88	129	0.10	0.11	0.12	0.13	0.07
RP2F03	81	80	68	84	69	0.16	0.15	0.13	0.12	0.13
RP2F04	81	75	92	91	76	0.28	0.34	0.10	0.15	0.11
Mean	84	82	93	85	90	0.18	0.19	0.11	0.14	0.10
S.D.	4	7	27	6	27	0.08	0.10	0.02	0.02	0.03
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 19

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	UN (mg/dL)					CRE (mg/dL)				
	UN (mg/dL)	UN (mg/dL)	UN (mg/dL)	UN (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CRE (mg/dL)	CRE (mg/dL)	CRE (mg/dL)	CRE (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	17.5	20.2	20.1	15.0	15.9	0.92	0.83	0.79	0.78	0.73
RP2F02	20.1	20.0	18.5	17.2	19.1	0.77	0.91	0.88	0.90	0.82
RP2F03	16.1	15.8	17.9	15.3	17.1	0.79	0.86	0.85	0.80	0.81
RP2F04	15.3	18.8	20.4	13.4	19.2	0.70	0.75	0.66	0.61	0.65
Mean	17.3	18.7	19.2	15.2	17.8	0.80	0.84	0.80	0.77	0.75
S.D.	2.1	2.0	1.2	1.6	1.6	0.09	0.07	0.10	0.12	0.08
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	CHO (mg/dL)					TG (mg/dL)				
	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	123	122	103	110	114	27	20	23	12	16
RP2F02	108	112	115	107	107	59	43	40	30	46
RP2F03	144	144	142	150	148	37	20	34	32	24
RP2F04	117	95	99	94	94	21	18	47	22	34
Mean	123	118	115	115	116	36	25	36	24	30
S.D.	15	20	19	24	23	17	12	10	9	13
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 21

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	PL (mg/dL)					IP (mg/dL)				
	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	146	141	146	139	162	4.05	4.86	1.84	4.83	1.72
RP2F02	161	161	160	148	160	2.69	4.02	4.83	4.50	3.75
RP2F03	181	183	203	198	188	4.13	3.75	3.37	3.56	3.53
RP2F04	122	129	134	122	144	3.91	3.12	1.69	3.46	2.51
Mean	153	154	161	152	164	3.70	3.94	2.93	4.09	2.88
S.D.	25	24	30	33	18	0.68	0.72	1.48	0.68	0.94
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	CA (mg/dL)					NA (mEq/L)				
	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	9.48	9.74	9.66	9.52	9.49	152.0	146.7	147.2	148.7	148.2
RP2F02	10.11	10.80	10.06	9.49	9.31	152.7	157.0	152.0	151.7	150.4
RP2F03	9.64	9.49	9.63	9.25	9.15	152.5	149.5	151.3	152.2	149.0
RP2F04	9.63	9.12	9.40	9.22	9.58	149.1	143.6	145.2	144.6	147.1
Mean	9.72	9.79	9.69	9.37	9.38	151.6	149.2	148.9	149.3	148.7
S.D.	0.27	0.72	0.27	0.16	0.19	1.7	5.7	3.3	3.5	1.4
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 23

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	K (mEq/L)					CL (mEq/L)				
	K (mEq/L)	K (mEq/L)	K (mEq/L)	K (mEq/L)	K (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	3.87	4.36	5.12	4.60	4.56	111.5	109.8	111.8	113.6	111.7
RP2F02	4.59	5.05	5.84	4.68	4.39	108.4	107.3	112.1	111.5	110.7
RP2F03	3.82	4.39	4.30	3.62	3.62	111.3	111.0	110.7	114.6	110.6
RP2F04	3.68	3.65	4.53	3.92	3.96	108.4	104.6	114.2	114.2	111.6
Mean	3.99	4.36	4.95	4.21	4.13	109.9	108.2	112.2	113.5	111.2
S.D.	0.41	0.57	0.69	0.52	0.42	1.7	2.8	1.5	1.4	0.6
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	TP (g/dL)					ALB (g/dL)				
	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	7.68	7.29	7.08	7.20	6.99	4.06	3.77	3.66	3.83	3.60
RP2F02	8.01	8.39	7.69	7.52	7.53	3.99	4.24	3.89	3.79	3.58
RP2F03	7.42	7.31	7.25	7.09	7.04	4.05	3.96	4.03	4.05	3.90
RP2F04	7.37	7.14	6.77	6.92	6.83	3.82	3.54	3.38	3.56	3.44
Mean	7.62	7.53	7.20	7.18	7.10	3.98	3.88	3.74	3.81	3.63
S.D.	0.29	0.58	0.38	0.25	0.30	0.11	0.30	0.28	0.20	0.19
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 25

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	A/G					T-BA ($\mu\text{mol/L}$)				
	A/G	A/G	A/G	A/G	A/G	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)	T-BA ($\mu\text{mol/L}$)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	1.12	1.07	1.07	1.14	1.06	0.5	1.2	15.3	2.6	1.3
RP2F02	0.99	1.02	1.02	1.02	0.91	5.1	3.0	3.1	1.3	3.1
RP2F03	1.20	1.18	1.25	1.33	1.24	4.1	5.2	4.5	4.7	5.5
RP2F04	1.08	0.98	1.00	1.06	1.01	0.5	1.9	20.4	1.8	19.4
Mean	1.10	1.06	1.09	1.14	1.06	2.6	2.8	10.8	2.6	7.3
S.D.	0.09	0.09	0.11	0.14	0.14	2.4	1.7	8.4	1.5	8.2
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)
	-1	1	2	3	4
RP2F01	0.02	0.01	0.02	0.02	0.03
RP2F02	0.30	0.38	0.34	0.39	0.44
RP2F03	0.05	0.04	0.09	0.11	0.08
RP2F04	0.06	0.05	0.05	0.08	0.10
Mean	0.11	0.12	0.13	0.15	0.16
S.D.	0.13	0.17	0.15	0.16	0.19
N	4	4	4	4	4